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| Office Action Summary | Application No. 10/524,754 | Applicant(s) KASABOV ET AL. |
| | Examiner PABLO WHALEY | Art Unit 1631 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(o).

Status

- 1) Responsive to communication(s) filed on 06 February 2009.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-6 and 8-23 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1-6 and 8-23 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date 04/13/2009.
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date 01/23/09.
- 5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

Status of Claims

Claims 1-6 and 8-23 are pending.

Claims 1-6 and 8-23 are rejected.

Claim 7 is cancelled.

Priority

Neither the drawings nor the specification of Provisional Application No. 60/403,756, filed Aug. 15, 2002, provides support for a combined Class A/Class B output having greater accuracy than either Class A or Class B outputs individually, as in amended claims 1 and 3, filed 02/06/2009. Therefore applicants are not given benefit of priority to Provisional Application No. 60/403,756 for independent claim numbers 1, 3, and 23, and claims that depend from claims 1 and 3 in view of applicant's amendments, filed 02/06/2009.

Declaration

The Declaration filed 02/06/2009 by Nikola Kasabov under 37 CFR 1.132, which asserts that one of ordinary skill in the art would not know how to modify the teachings of Downs in view of Barnhill and Hemstreet for making medical decisions wherein said combined class A/class B output has greater accuracy than either class A or class B individually, has been fully considered but is moot in view of the new grounds of rejections.

Information Disclosure Statement

The information disclosure statement filed 04/13/2009 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has

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not been considered. In order to correct this issue, applicant must provide a legible copy of each cited foreign patent document and non-patent literature publication or that portion which caused it to be listed.

Withdrawn Rejections

The rejection of claims 1-6 and 8-17 under 35 U.S.C. 101, is withdrawn in view of applicant's amendments, filed 02/06/2009.

The rejection of claims 1-6 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Downs in view of Barnhill and Hemstreet is withdrawn in view of applicant's amendments, filed 02/06/2009.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8-17, 19, 20, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharpe et al. (1993, Clinical Chemistry, Vol. 39. No. 11, p.2248-2253), in view Barnhill et al. (US 5,769,074; Issued Jun. 23, 1998), in view of Kasabov (WO/2001/078003; Published: 18 October 2001),

and in view of Wu et al. (Neural Networks, 2004, Proceedings. 2004 IEEE International Joint Conference, Published: 25-29 July 2004, Volume: 3, p. 2437- 2442).

This rejection is necessitated by applicant's amendment, filed 02/06/2009, which now requires a combined Class A/Class B output having greater accuracy than either Class A or Class B outputs individually.

Sharpe teaches a computer platform suitably programmed to perform medical decision support for thyroid diagnosis [Abstract and p.2250, Software]. A plurality of different types of clinical data is provided as input to a neural network [Table 1]. A schematic diagram shows neural networks comprising input neurons, classification modules, and output modules [Fig. 1, Fig. 2, Fig. 3, p.2250, Col. 1], which shows a plurality of input modules for acquiring data and classifying data. One-output and two-output modules are provided, wherein each output is a linear combination of weighted inputs [Fig. 1, Fig. 2, Fig. 3, p.2251], which shows combined class outputs. Connection weights are assigned values between 0 and 1 [p.2251, Col. 1]. Error values are produced during the training process and used to minimize the output error [p.2249, Col. 2, ¶3], which shows minimizing error such that output has greater accuracy. The system classifies relationships between thyroid analysis values and diagnostic classifications using multilayer perceptrons and provides diagnostic groups [p.2249, Col. 2, p.2250, Col. 1, ¶2, p.2251, Col. 1], which shows classes and medical outcomes. Sharpe suggests the use of additional software to confirm and validate input data and point out errors in advice to the user [p.2253, Col. 1, ¶2].

Sharpe does not specifically teach the use of gene expression data as input, as in claims 1, 3, 5, and 8.

Sharpe does not specifically teach combined equations for Class A, Class B, and Class A/Class B with greater accuracy than either Class A or Class B, as in claims 1, 3, and 23.

Sharpe does not specifically teach connection weight values for beta 1, beta 2, and alpha, as in claims 1, 3, and 23.. However, it would have been obvious to one of ordinary skill in the art to substitute connection weights using any desired mathematical variable with predictable results, since this is an arbitrary design parameter.

Sharpe does not specifically teach an evolving connectionist neural network system [Fig. 2], as in claims 11 and 21.

Sharpe does not specifically teach a Bayesian process for minimizing error, as in claim 22.

Kasabov teaches a neural network module for adaptive decision support. In particular, gene expression data is used as input into the network for classification [p. 23, last ¶, p.24]. Kasabov teaches an adaptive component that represents connection weights as a summation of nodes and classes [p.8, lines 20-bottom, p.9, lines 1-15]. An error minimization scheme is presented in order to achieve better prediction accuracy [p.19, lines 5-32]. Kasabov also shows an evolving connectionist neural network system [Fig. 2, p.¶3], as in claim 11. This system provides improved recognition in a noise environment [p.24, ¶5].

Barnhill teaches a method for predicting medical outcomes that can use a combination of both biomarker data predictive of disease and patient data as input into a neural network [Fig. 4, Col. 14, ¶1, Col. 17, ¶1, Col. 18, ¶3, Col. 20], including gene markers which suggests gene expression data. A final diagnostic index is provided (i.e. output) that is a combination of biomarker analysis and other non-numerical patient information [Col. 14, ¶1]. The system also provides four-output groups [Fig. 1] and interrelation layers [Fig. 2], and means for graphically displaying results [Col. 14, ¶2, ¶4].

Wu teaches neural network fusion strategies for classifying tumors [Introduction]. In particular, Wu shows fusing individual outputs of classifiers to arrive at a consensus decision using ensemble strategies [Introduction, p.2437, Col. 2]. Ensemble strategies are described in detail and includes Bayes, perceptron averaging, and weighted averaging [p.2437, Col. 2, p.2438, Col. 1, and Section III], wherein

outputs are minimized using specific functions [Equations 4-8]. Wu also shows that the ensemble outputs provides significant improvements over individual neural network outputs [p.2440, Col. 2, Table I]. This technique is beneficial for improving classification performance [p.2437, Col. 2, ¶4, p.2438, Section II].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Sharpe by incorporating gene expression data, as in claims 1, 3, 5, 8, and 23, since Kasabov shows gene expression data used in neural networks, and since Barnhill suggests gene expression data can be successfully combined with clinical patient data for medical decision support with predictable results, as shown above. The motivation would have been to increase diagnostic power by combining qualitative and quantitative data, as suggested by Barnhill [Col. 17, ¶1].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Sharpe by determining equations for a combined Class A output and a combined Class B output, as in claims 1, 3, and 23., since Barnhill shows multiple outputs based on linear combinations of connection weights and different types of input data, as set forth above, and since Kasabov shows that adjustments to output represented by changes in connection weights based on linear combinations of different classes [p.8, lines 20-bottom, p.9, lines 1-15]. The motivation would have been to improve decision support by using error minimization schemes to achieve better prediction accuracy [p. 7, last ¶, p.19, lines 5-32].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Sharpe by calculating a combined class A/class B output with an error that is minimized and an accuracy that is greater than either class A or class B individually, as in claims 1, 3, and 23, or a Bayes process, as in claim 22, since Wu shows fusing individual outputs of classifiers to arrive at a consensus decision [Introduction, p.2437, Col. 2] and ensemble strategies including a Bayes process [p.2437, Col. 2, p.2438, Col. 1]. The motivation would have been to provide

significant improvements over individual neural network outputs to improve classification performance, as suggested by Wu [p.2440, Col. 2, p.2437, Col. 2, ¶4, p.2438, Section II].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention of Sharpe by using an evolving connectionist or fuzzy neural network system [Fig. 2], as in claims 11 and 21, since Kasabov also shows an evolving connectionist neural network system for decision support [Fig. 2]. The motivation would have been to provide improved classification in a high-noise environment, as suggested by Kasabov [p.24, ¶5].

Claims 1-6 and 8-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharpe et al. (1993, Clinical Chemistry, Vol. 39. No. 11, p.2248-2253), in view Barnhill et al. (US 5,769,074; Issued Jun. 23, 1998), in view of Kasabov (WO/2001/078003; Published: 18 October 2001), and in view of Wu et al. (Neural Networks, 2004, Proceedings. 2004 IEEE International Joint Conference, Published: 25-29 July 2004, Volume: 3, p. 2437- 2442), as applied to claims 1-6, 8-17, 19, 20, 21, and 22, above, and further in view of Tsumoto (Information Sciences, 1998, Vol. 112, p.67-84).

Sharpe, Barhnill, Kasabov, and Wu make obvious a computer platform suitably programmed to perform medical decision support, as set forth above.

Sharpe, Barhnill, Kasabov, and Wu do not specifically teach an exhaustive search strategy for minimizing error, as in claim 18.

Tsumoto teaches expert system learning rules for making medical decisions [Abstract]. In particular, probabilistic rules are described for predicting medical diagnosis that includes an accuracy measure [p.71]. Also described is an exhaustive search algorithm for eliminating candidates to increase prediction power [p.73, Section 4.1, 4.2], which shows improving accuracy of the result.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the invention made obvious by Sharpe, Barhnill, Kasabov, and Wu alternatively using an exhaustive search strategy for minimizing error, as in claim 18, since Tsumoto shows an exhaustive search algorithm for eliminating candidates to increase prediction accuracy [p.71, p.73, Section 4.1, 4.2]. The motivation would have been to improve decision making using additional software to confirm and validate input data and point out errors in advice to the user, as suggested by Sharpe [p.2253, Col. 1, ¶2].

Response to Arguments

Applicant's arguments, filed 02/06/2009, that one of ordinary skill in the art would not know how to modify the teachings of Downs in view of Barnhill and Hemstreet for making medical decisions wherein said combined class A/class B output has greater accuracy than either class A or class B individually, as in amended claims 1 and 3, have been fully considered but are moot in view of the new grounds of rejections.

Applicant's arguments, filed 02/06/2009, that Barnhill does not provide any enabled methods for improving accuracy of a combined Class A/Class B output have been fully considered but are moot in view of the new grounds of rejections.

The Declaration filed 02/06/2009 by Nikola Kasabov under 37 CFR 1.132, which asserts that one of ordinary skill in the art would not know how to modify the teachings of Downs in view of Barnhill and Hemstreet for making medical decisions wherein said combined class A/class B output has greater accuracy than either class A or class B individually, has been fully considered but is moot in view of the new grounds of rejections.

In addition, the Declaration asserts that the claimed invention results in improved accuracy [p.2, last ¶]. However, it is well settled that unexpected results must be established by factual evidence. Applicants have not presented any experimental data showing that the claimed process results in an unexpected result

of improved accuracy. Due to the absence of tests comparing applicant's claimed method steps with those of the closest prior art, applicant's assertion of unexpected results constitute mere opinion evidence. See also *In re Linder*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972); *Ex parte George*, 21 USPQ2d 1058 (Bd. Pat. Appl. & Inter. 1991). In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pablo S. Whaley

Patent Examiner

Art Unit 1631

/PW/

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Primary Examiner, Art Unit 1631